



US005762904A

**United States Patent** [19][11] **Patent Number:** **5,762,904**

Okada et al.

[45] **Date of Patent:** **Jun. 9, 1998****[54] ORAL DELIVERY OF VACCINES USING POLYMERIZED LIPOSOMES**

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[21] Appl. No.: **786,617**[22] Filed: **Jan. 17, 1997****Related U.S. Application Data**

[63] Continuation of Ser. No. 96,689, Jul. 23, 1993, abandoned.

[51] **Int. Cl.<sup>6</sup>** ..... **A61K 9/127**; A61K 39/00;  
A61M 36/12[52] **U.S. Cl.** ..... **424/1.21**; 264/4.1; 264/4.3;  
424/9.321; 424/9.4; 424/9.51; 424/9.6;  
424/184.1; 424/278.1; 424/450; 424/812;  
428/402.2[58] **Field of Search** ..... 424/450, 1.21,  
424/9.321, 9.51, 184.1, 812, 278.1, 9.4,  
9.6; 428/402.2; 264/4.1, 4.3**[56] References Cited****U.S. PATENT DOCUMENTS**

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**[57] ABSTRACT**

Polymerized liposomes, methods of preparing the polymerized liposomes and incorporating biologically active substances within the polymerized liposomes, and methods of administering polymerized liposomes containing a biologically active substance to be delivered to a patient are disclosed. The polymerized liposomes are prepared by polymerizing double bond-containing liposomes. The polymerization can be initiated with a source of radiation and/or a free radical initiator. Biologically active substances can be incorporated into both the hydrophilic and hydrophobic layers of the liposomes, either during or after polymerization. The polymerized liposomes can be administered orally to a patient in need of the biologically active substance to be delivered. Examples demonstrate enhanced stability.

**13 Claims, 4 Drawing Sheets**